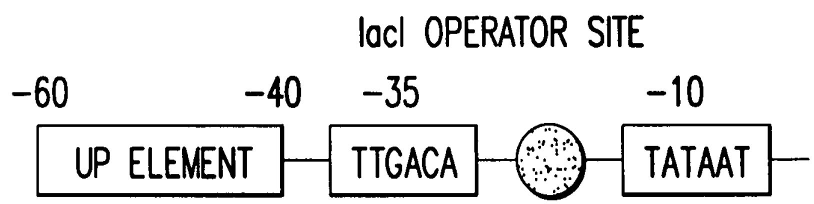


FIG.1A

5'–GATCCT*CAGAAAATTATTTTAAATTT*CCAATTGACA*TTGTGAGCGGATAACAAT*ATAATGTGTGGA

UP ELEMENT -35 ELEMENT Lac OPERATOR -10 ELEMENT

FIG.1B

5'AGAAAGCAAAAATAAATGCTTGACACTGTAGCGGGAAGGCGTATA
ATGGAATTGTGAGCGGATAACAATTCACA 3'

FIG.1C

ACTCGCGGA TCATCTTCAC CATCGGCCGC AACTCCTGCG
GGATATCCTC GTCCTCCTCC TCCACCGGCA CCCCCATGGT AGCGGCCAGC-
TCGCGCCCTG CCTGGGAAAG CTGTACATGC TGATCGGCGG CGTCGGTGCC
GGCGGCCGGG TCTTCCGCCT GCTCGGCGGT GCCGGTCCGT GCGGCCTTGG
CGTCCGCGGC GGCGCGCGAT GAGGGCGGCA CCTGGGTGGT GATCCAGCCA
CTGAGGGTCA ACATTCCAGT CACTCCGGGA AAAATGGAAT TCTTCCATTG
GATCGGCCCA CGCGTCGCGA ACTTGAGCCC CCTTTTCGTC GCCCCTTGAC
AGGGTGCGAC AGGTAGTCGC AGTTGTTTGA CGCAAGTCAC TGATTGGAAA
CGCCATCGGC CTGTCAGAAA TGGTCGTTGCC AGACCTATGG CTGGCACCCG
CATCGCGGCT GCGTTACCCT TACTCCTGTT GTGCCTTTAA CCTAGCAAGG AC

FIG.1D

AATTCCTCGA AGTCCTTGCG CTGCTTGTCG TTCATGATGT
CGTAGATCAG CGCATGCACC TGCTTGTGTT CCAGCGGTGG CAGGTTGATC
CGGCGTACAT CGCCATCCAC CCGGATCATG GGTGGCAGGC CGGCGGAGAG
GTGCAGGTCC GAAGCGCCCT GTTTGGCACT GAAGGCGAGC AGCTCGGTAA
TATCCATGGG ACTCCCCAAT TACAAGCAAG CAGGTAGAAT GCCGCCAAAG
CCGCCGTCTC GGACAAGGAA AACACCGGAT GAGCCAGGGT GCTTCCAGGA
CACGCGTGGT GTCCTGCGCC AGACGCGGAA CCTCGACACT GGAACAGGAA
GATGGCCATC GAGGCCGGCG GTTTCGAGGG CGTCGAGCCG ACGCCGACCG
CACTTCCATA GGGCGCAGGT AATGTCCACG ATAGCAGAGA ATATTGCAAA
GGTTGCCGCG CGCATCCGTG AGGCAGCGCA AGCTGCGGGG CGCGATCCGG
CCACGGTCGG CCTGCTCGCC GTGAGCAAGA CCAAGCCCGC CGCCGCGGTG
CGCGAGGCGC ACGCCGCCGG CCTTCGCGAC TTCGGCGAAA ACTACCTGCA
GGAGGCCCTC GGCAAGCAGG CCGAACTGGC CGACCTGCCC TTGAACTGGC
ACTTCATCGG CCCCATCCAG TCGAACAAGA CGCGGCCCAT CGCCGAGCAT
TTCCAGTGGG TGCACTCCGT GGACCGGTTG AAGATCGCGC AGCGCCTGTC
GGAGCAACGC CCGGCCGGGC TGCCGCCCCT GAATGTCTGC CTGCAGGTCA
ACGTCAGCGG CGAAGCCAGC AAGTCCGGCT GCGCCCCCGA GGACCTGCCG
GCCCTGGCCG AGGCCGTGAA GCAACTGCCC AACCTCCGAT TGCGTGGCCT
GATGGCCATC CCCGAACCCA CCGCCGAACG CGCCGCGCAA CACGCCGCGT
TCGCCCGCCT GCGCGAACTG CTGCTGGACC TGAACCTTGG CCTGGACACC
CTGTCCATGG GCATGAGCGA CGACCTCGAG GCAGCCATCGG CGAAGGTGCG
ACCTGGGTCC GCATCGGTAC CGCCCTGTTC GGCGCCCGCGA CTACGGCGCG
CCGGCTTCTT GAATGAATCCC

FIG.1E

CTAGAGCTAT TGATGTGGAT CAACATTGTC CACTAGCCGC
TGCCGCCTAA TCTCCAGAAT TGTGAG

FIG.1F

```
   1 ttatttagca ggaataatta gccagattat cgagggagtt ccagggcaatccaaacattg
  61 ttatatatgc atttataaaa ttttcaagat aatttattat tcataccttgccctttgtt
 121 tcaaaattat gccctttttt tgcccttgga aacaaccaca ctcctaaattaataggtggt
 181 gtggtttgat catttataat ataacataaa aacaaccacc cagtaactagtatgagtggc
 241 gtagcgacta taacaactct atgttatcaa gatatatgta tatgagtgatgacaaggaag
 301 atgtctcctg tgagaccaac agccagatat atggcctctt gccgggctatatagttcact
 361 cctactatat acacatgtaa ttataacata aaaaaataga caagtaccgaagtacctgcc
 421 taaataacaa caagattaac atgtgaataa tggaaataaa aagtcacgcccgaaggctaac
 481 ttacgaatag atgaaaattt gaacacattg ctgtgtctaa aatgattatagcataaataa
 541 cgaatatttc cagctcgaaa ttaatatatt gtaataataa tattttatatctttgttaat
 601 aattatttaa ttgatttaca taaataataa ttgtaaaatt aatttgtaatcgattgcaaa
 661 taagttatag gagaaaataa aatgaataaa aaactattaa caaaaacattgatagcaagt
 721 gctttagttt taacaacagt aggttcaggt tttcattctt cttcaaattataatggtatt
 781 aataacgttg aaaaagctga gcaaacgaca gataacgcat tgtggaaaatgtaagagac
 841 gctttaaaag acgcgaatat tatcgataaa acagataatg aaaatgtcaaggttacgtat
 901 aaaatagaaa atggtggaga aaataccata gaaggaacag ttaatttagaaaatattagt
 961 acttcaaaca atcctaaaat aaaccctcaa aatgttacaa aaattaatataactagaaaa
1021 aatccgaact accctaatat tgatgctaat aatacatgga aaaaattaccagaaaaattg
1081 aaagaaaaaa atatagtgga acaacggcga caatgtttca atcttaagtacagaccctaa
1141 agatgagact gtattcggta aagtaggaga agataaatca aacgtaagcaatagatacat
1201 caatcctaaa gatataaatg aattcaaatc actaaaaata ctttttccgaggcagatta
1261 ctcctgcctc tttctttgaa cagtgatatc ttctgatcta tgtaacactcaattacttca
1321 gattctttac ctttaacttc ctttaattca tttctctcta tctcctcaaaagttgtgct
1381 ttttgatttg tgattggagt tgggcgtttt ttcatcgcgt tgtttcaattccttttttaag
1441 gtattctaat tctcttctag tcatatcaat tgttttttta cttctcacctttagtgaaat
1501 actcttatcc tttctcttct tgcgttaatg ttgctaatta gtataaaatacatgcgccca
1561 tatattccaa tggtaggaca tttaattctg gattttcagc tattttcataaatctattat
1621 ctgataattt gcttaatcca attttcaagc catagcctaa attccccatccactaagtca
1681 ttttgtttca tatggtttta atctacggcc aatctcaaag atagattgaccagcgatgtt
1741 taaagtcata tttcacggat ccacatttac gataaacata tctagttacacaatattatc
1801 ccttactgca acacaggacg tttctcagcg taaaaaacac cactagaaagtgactttaaa
1861 gaatataact aattcaaact tatattaatt aatattcttt aaatgaccactcacactttg
1921 tttttgcta tttgtaactt taaaatgttg tttgaaatct atattttttgatatagctc
1981 cctatgtaac aaacaatttt taattaatat atatttaaac aagtcaatttagagatcggt
2041 taattcgatt catttaaata atatttatac attctatatg taaacgtttacacatttgaa
2101 gtaaggagaa ttaaaaatga
```

FIG.1G

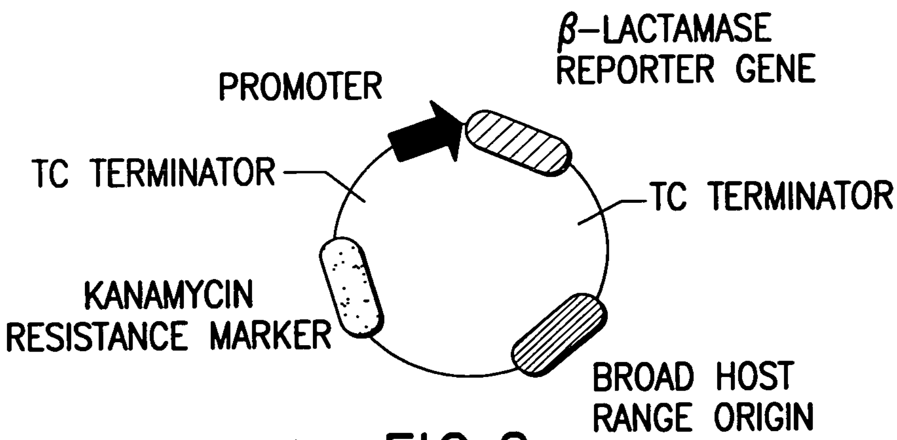


FIG.2

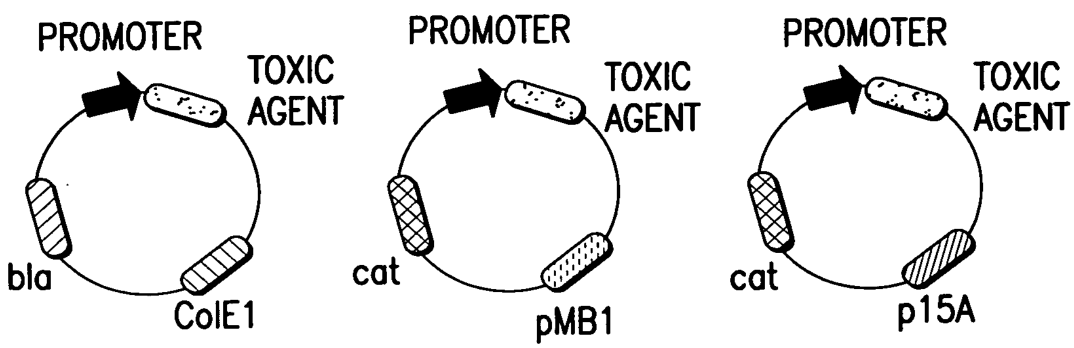


FIG.3A

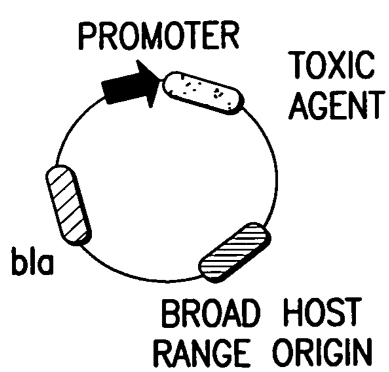


FIG.3B

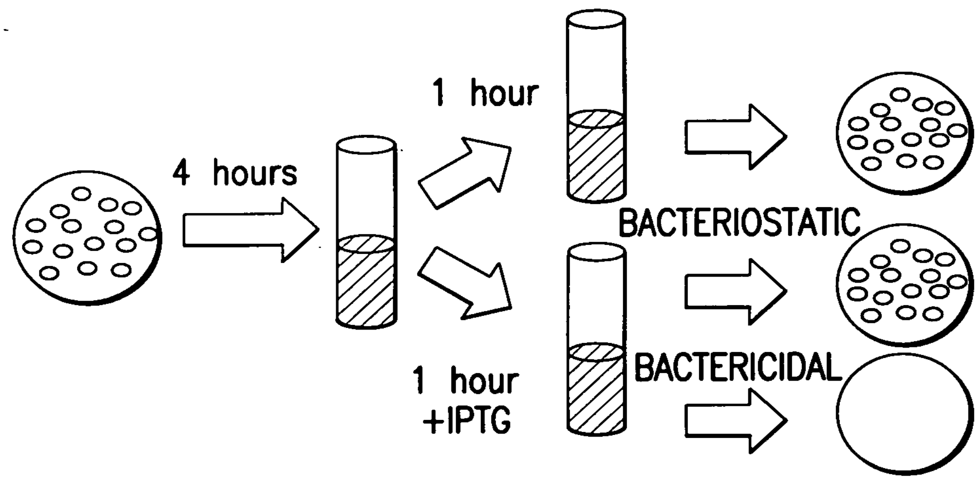


FIG.4

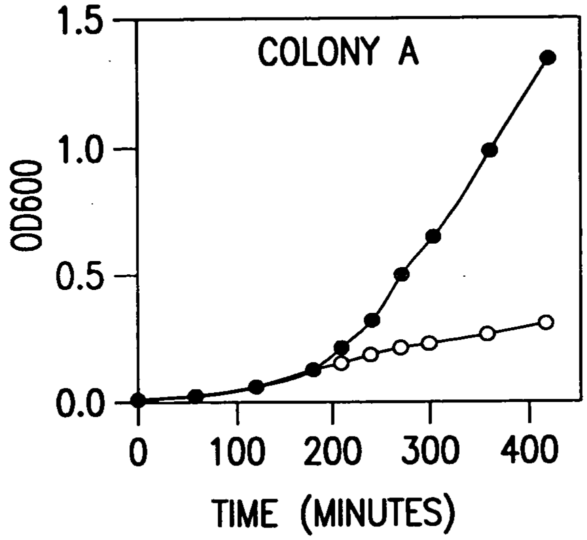


FIG.5A

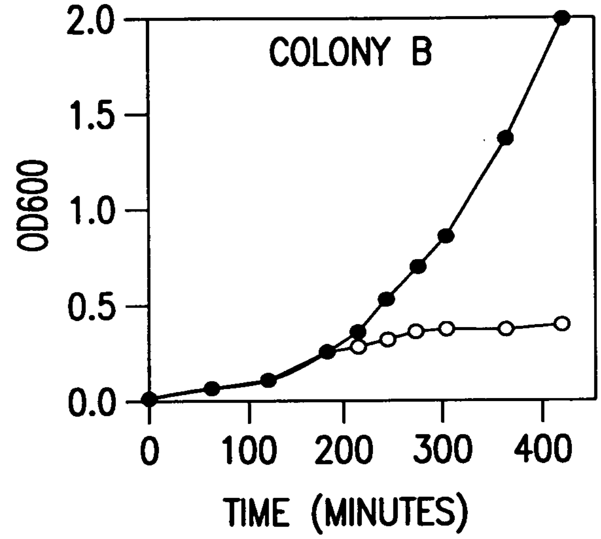


FIG.5B

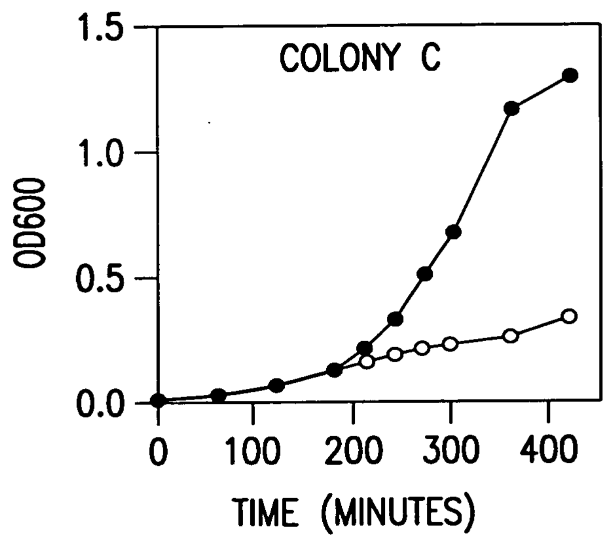


FIG.5C

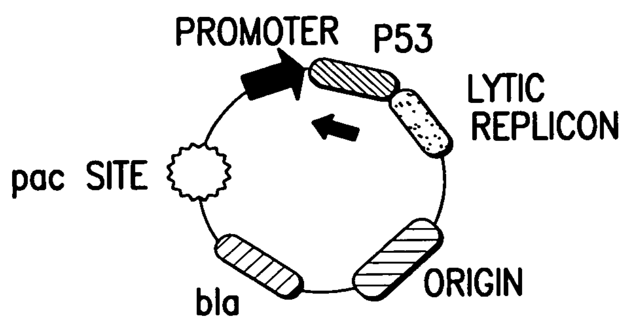

PROMOTER
P53
LYTIC
REPLICON
pac SITE
ORIGIN
bla

FIG.6A

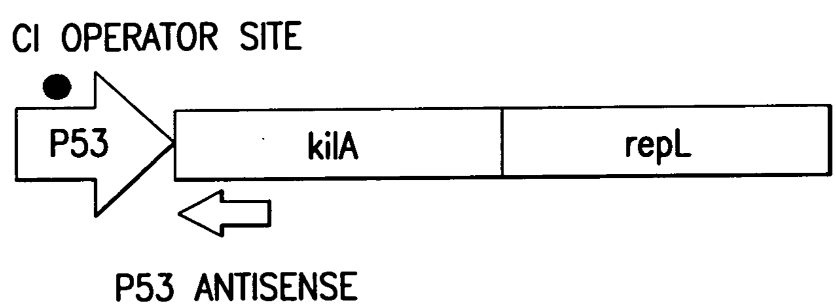

CI OPERATOR SITE
P53
kilA
repL
P53 ANTISENSE

FIG.6B

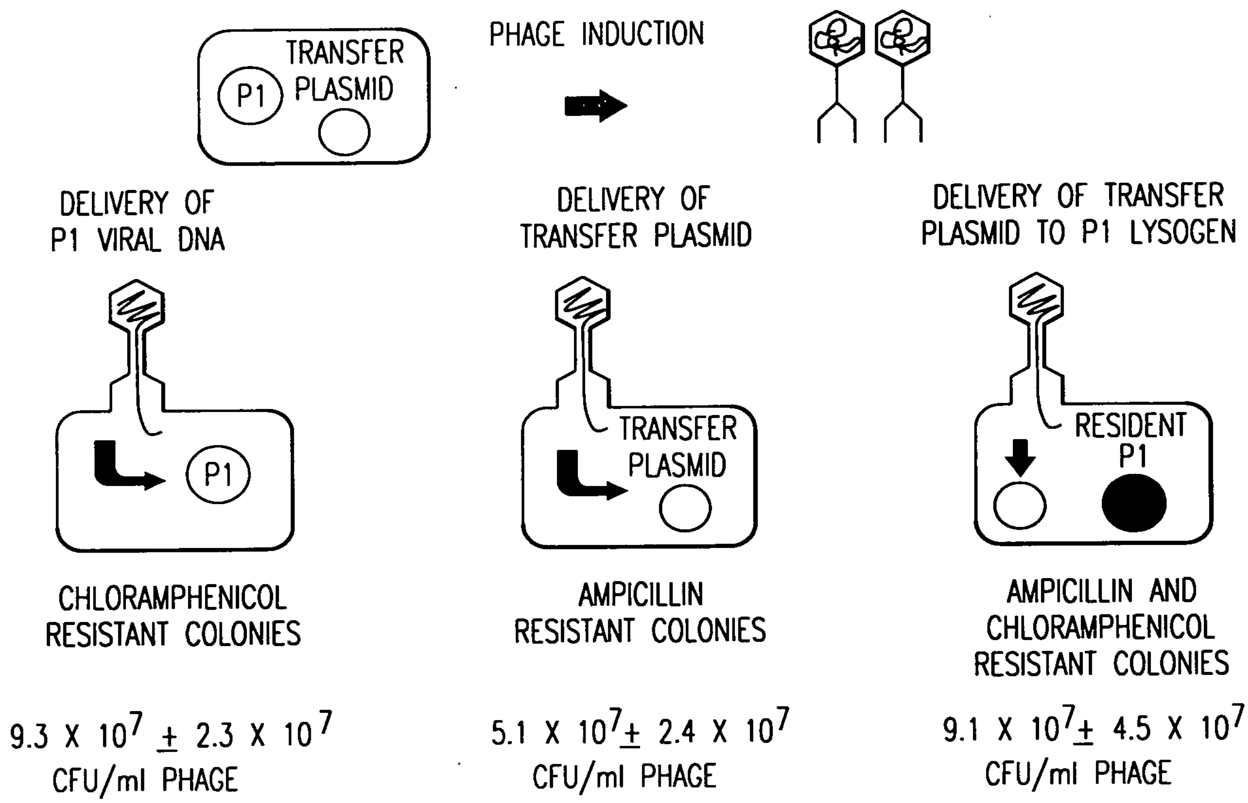

P1
TRANSFER PLASMID
PHAGE INDUCTION
DELIVERY OF P1 VIRAL DNA
DELIVERY OF TRANSFER PLASMID
DELIVERY OF TRANSFER PLASMID TO P1 LYSOGEN
P1
TRANSFER PLASMID
RESIDENT P1
CHLORAMPHENICOL RESISTANT COLONIES
AMPICILLIN RESISTANT COLONIES
AMPICILLIN AND CHLORAMPHENICOL RESISTANT COLONIES
9.3 X 10^7 ± 2.3 X 10^7 CFU/ml PHAGE
5.1 X 10^7 ± 2.4 X 10^7 CFU/ml PHAGE
9.1 X 10^7 ± 4.5 X 10^7 CFU/ml PHAGE

FIG.7

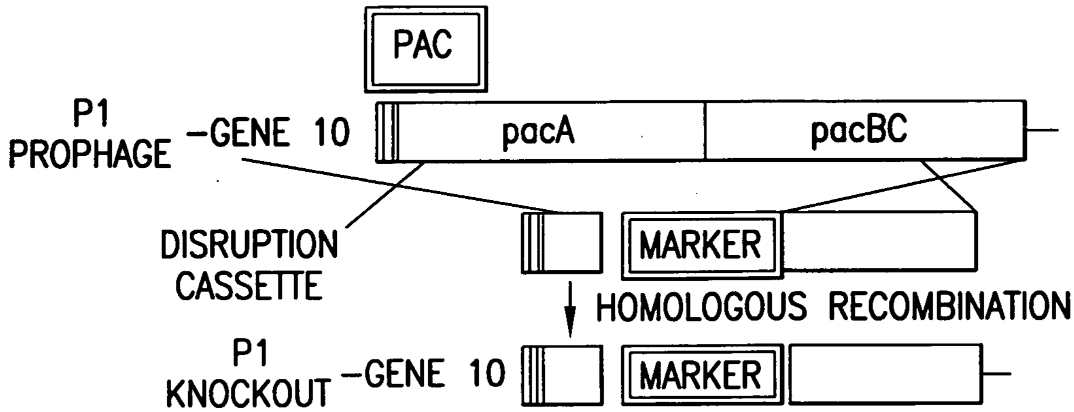

PAC
P1
PROPHAGE
-GENE 10
pacA
pacBC
DISRUPTION
CASSETTE
MARKER
HOMOLOGOUS RECOMBINATION
P1
KNOCKOUT
-GENE 10
MARKER

FIG.8

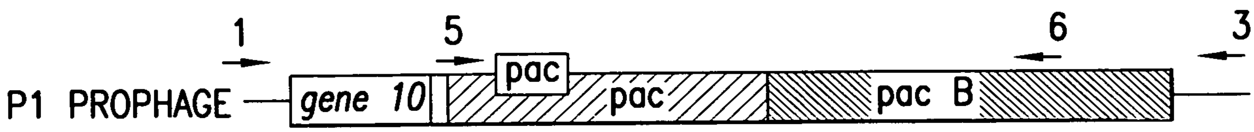

1
5
6
3
P1 PROPHAGE
gene 10
pac
pac
pac B

FIG.9A

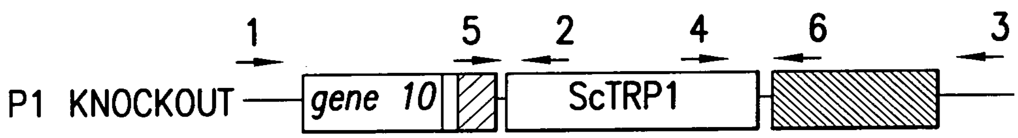

1
5
2
4
6
3
P1 KNOCKOUT
gene 10
ScTRP1

FIG.9B

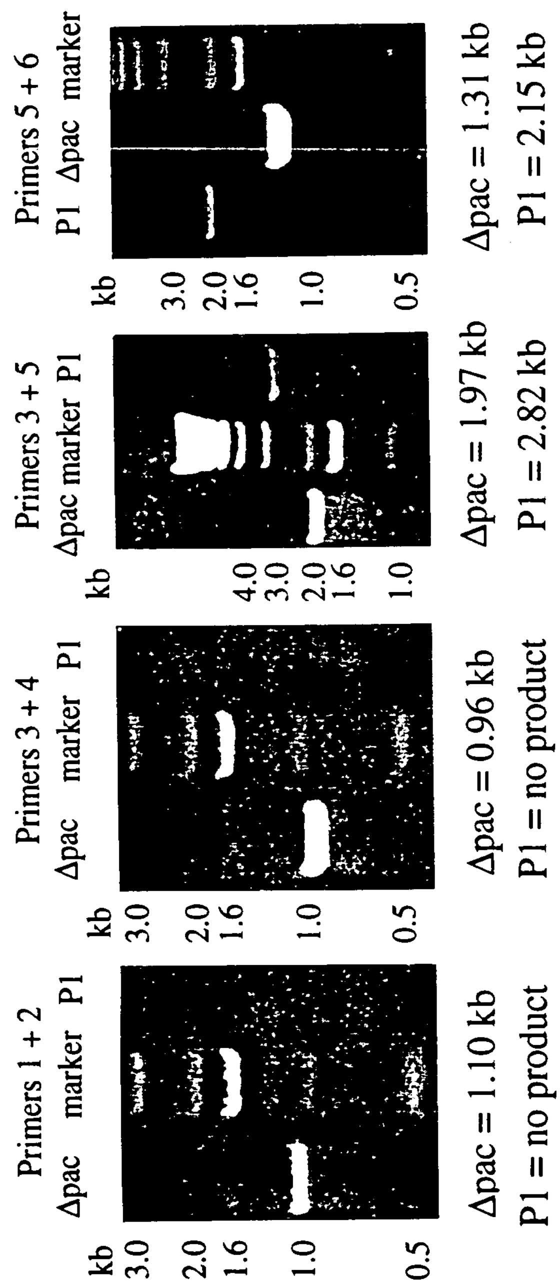
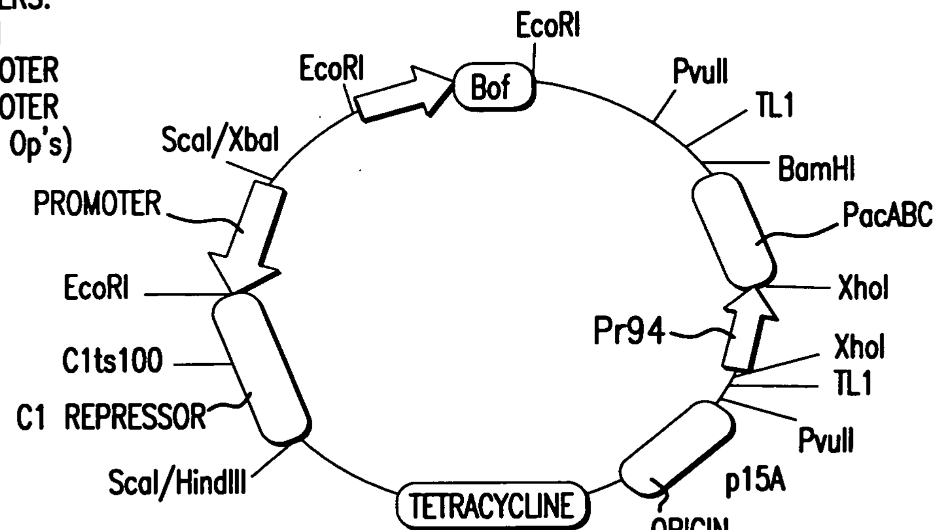

Primers 1 + 2
Δpac marker P1
kb 3.0 2.0 1.6 1.0 0.5
Δpac = 1.10 kb
P1 = no product
Primers 3 + 4
Δpac marker P1
kb 3.0 2.0 1.6 1.0 0.5
Δpac = 0.96 kb
P1 = no product
Primers 3 + 5
Δpac marker P1
kb 4.0 3.0 2.0 1.6 1.0
Δpac = 1.97 kb
P1 = 2.82 kb
Primers 5 + 6
P1 Δpac marker
kb 3.0 2.0 1.6 1.0 0.5
Δpac = 1.31 kb
P1 = 2.15 kb

FIG.9C

PAC DELETION COMPLEMENTING PLASMID

1) INACTIVATION OF C1 REPRESSOR BY TEMPERATURE SWITCH
2) DEREPRESSION OF Pr94 PROMOTER
3) EXPRESSION OF PacABC
4) PRODUCTION OF PACASE ENZYMES
5) CLEAVAGE OF *pac* SITE ON TRANSFER PLASMID

PROMOTERS:
pEDI
CI PROMOTER
CI PROMOTER
(MUTATED Op's)



PR94:
C1 REPRESSOR BINDING SITE OVERLAPS −35
COMPLETE REPRESSION REQUIRES Bof & C1 REPRESSOR
PROMOTER NORMALLY REPRESSED DURING LYSOGENIC GROWTH.
SWITCHED ON APPROXIMATELY 15' AFTER PROPHAGE

Bof MODULATOR:
FORMS TEMARY COMPLEX
C1 REPRESSOR•BOF•DNA
INCREASES EFFICIENCY OF C1 REPRESSION
DOES NOT BIND TO DNA ALONE

FIG.10

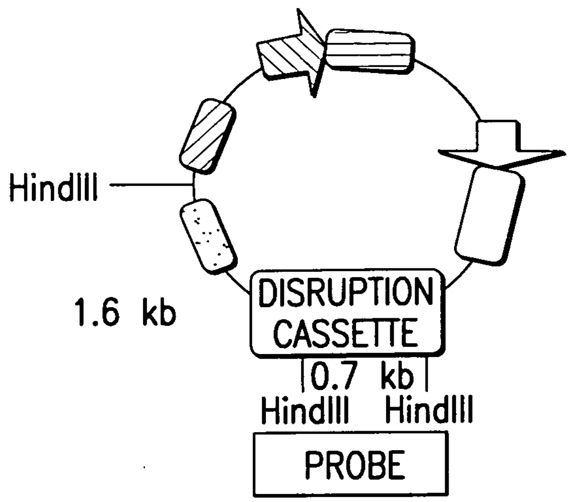

HindIII
1.6 kb
DISRUPTION CASSETTE
0.7 kb
HindIII
HindIII
PROBE

FIG.11A

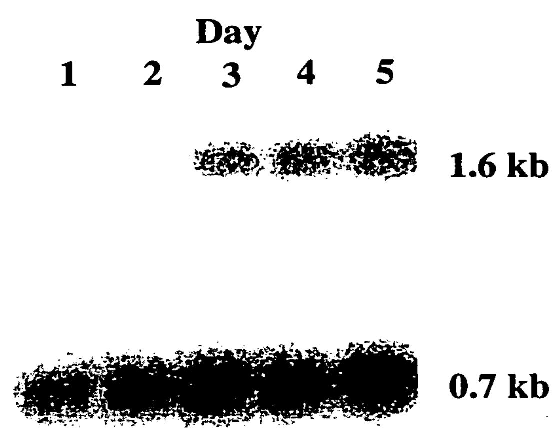


FIG.11B

```
                   a  a  c          c  c              g  c
CCACTAAAAAGCATGATCATTGATCACTCTAATGATCAACATGCAGGTGATCACATTGCG
Pro Leu Lys Ser Met Ile Ile Asp His Ser Asn Asp Gln His Ala Gly Asp His Ile Ala

                   g  g  g  g
GCTGAAATAGCGGAAAAACAAAGAGTTAATGCCGTTGTCAGTGCCGCAGTCGAGAATGCG
Ala Glu Ile Ala Glu Lys Glu Arg Val Asn Ala Val Val Ser Ala Ala Val Glu Asn Ala
               AATCAANNANTTA

                           c  c        c  c        t  t
AAGCGCCAAAATAAGCGCATAAATGATCGTTCAGATGATCATGACGTGATCACCCGC
Lys Arg Gln Asn Lys Arg Ile Asn Asp Arg Ser Asp Asp His Asp Val Ile Thr Arg
```

FIG.12

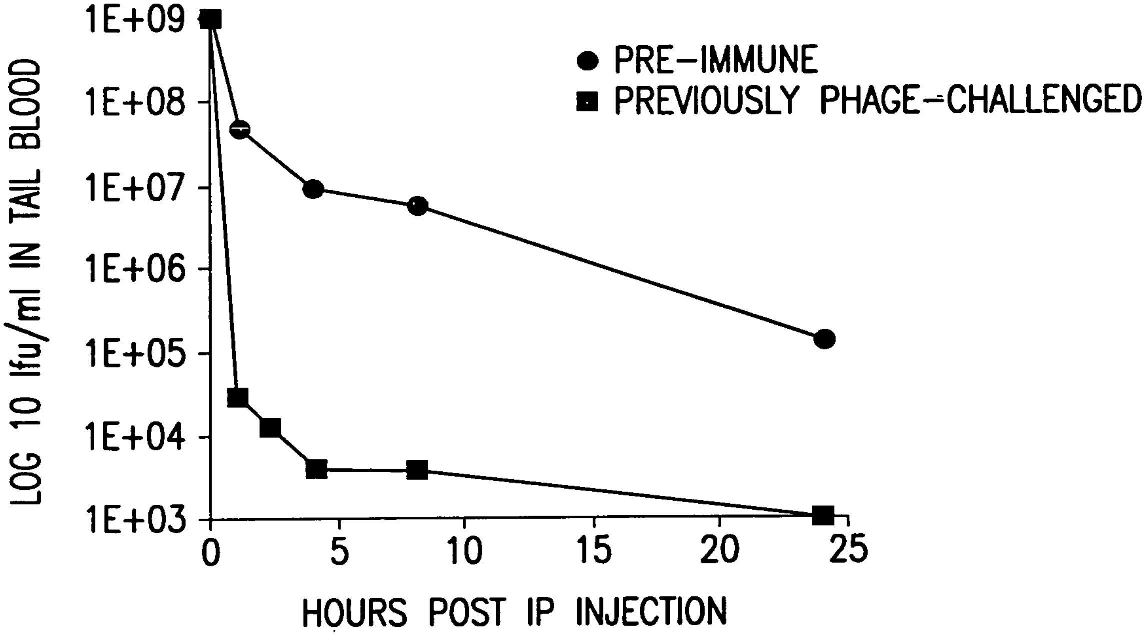
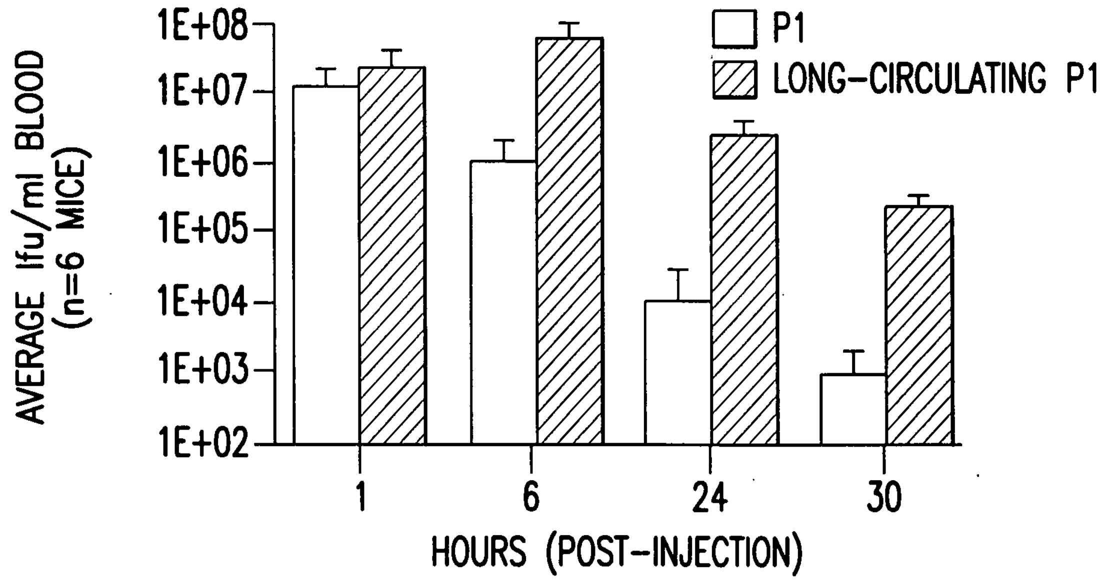

1E+09
1E+08
1E+07
1E+06
1E+05
1E+04
1E+03
LOG 10 lfu/ml IN TAIL BLOOD
PRE-IMMUNE
PREVIOUSLY PHAGE-CHALLENGED
0
5
10
15
20
25
HOURS POST IP INJECTION

FIG.13



HOURS POST-INJECTION	P1 (MEAN Ifu/ml BLOOD)	LONG-CIRCULATING P1 (MEAN Ifu/ml BLOOD)	FOLD IMPROVEMENT
1	1.29E+07	2.34E+07	2
6	1.13E+06	6.29E+07	56
24	1.12E+04	2.79E+06	249
30	1.00E+03	2.33E+05	233

FIG.14

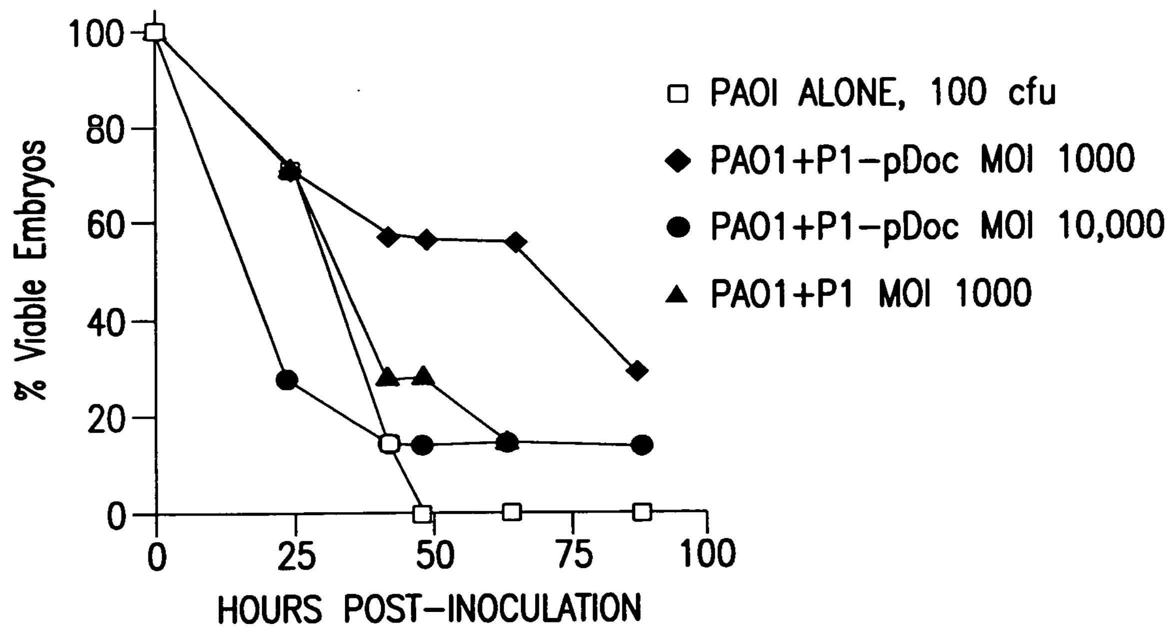

% Viable Embryos
100
80
60
40
20
0
0
25
50
75
100
HOURS POST-INOCULATION
PAOI ALONE, 100 cfu
PA01+P1-pDoc MOI 1000
PA01+P1-pDoc MOI 10,000
PA01+P1 MOI 1000

FIG.15

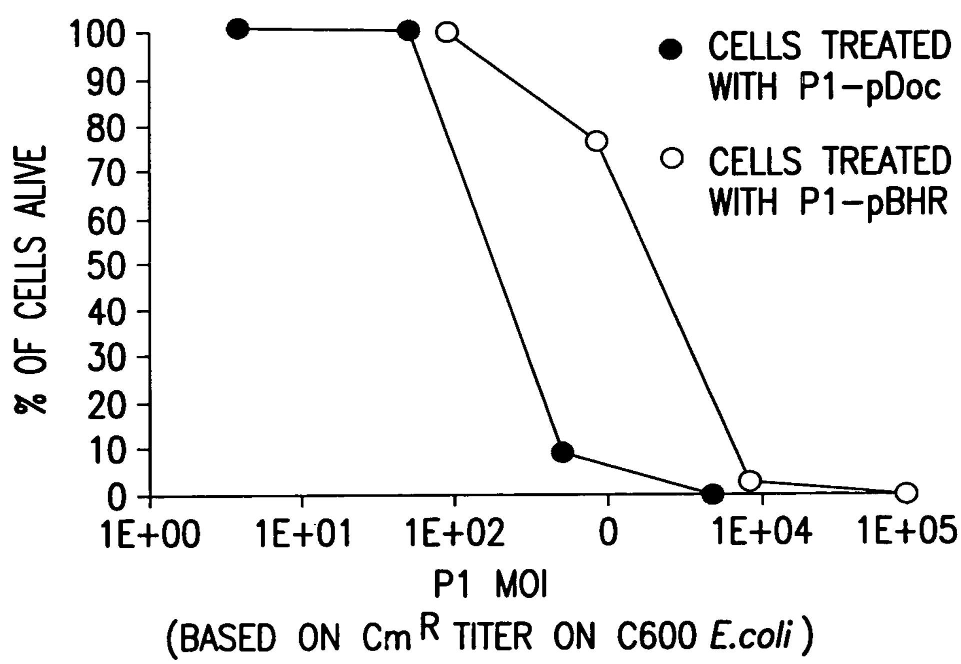

% OF CELLS ALIVE
100
90
80
70
60
50
40
30
20
10
0
1E+00
1E+01
1E+02
0
1E+04
1E+05
P1 MOI
(BASED ON Cm R TITER ON C600 E.coli)
CELLS TREATED WITH P1-pDoc
CELLS TREATED WITH P1-pBHR

FIG.16

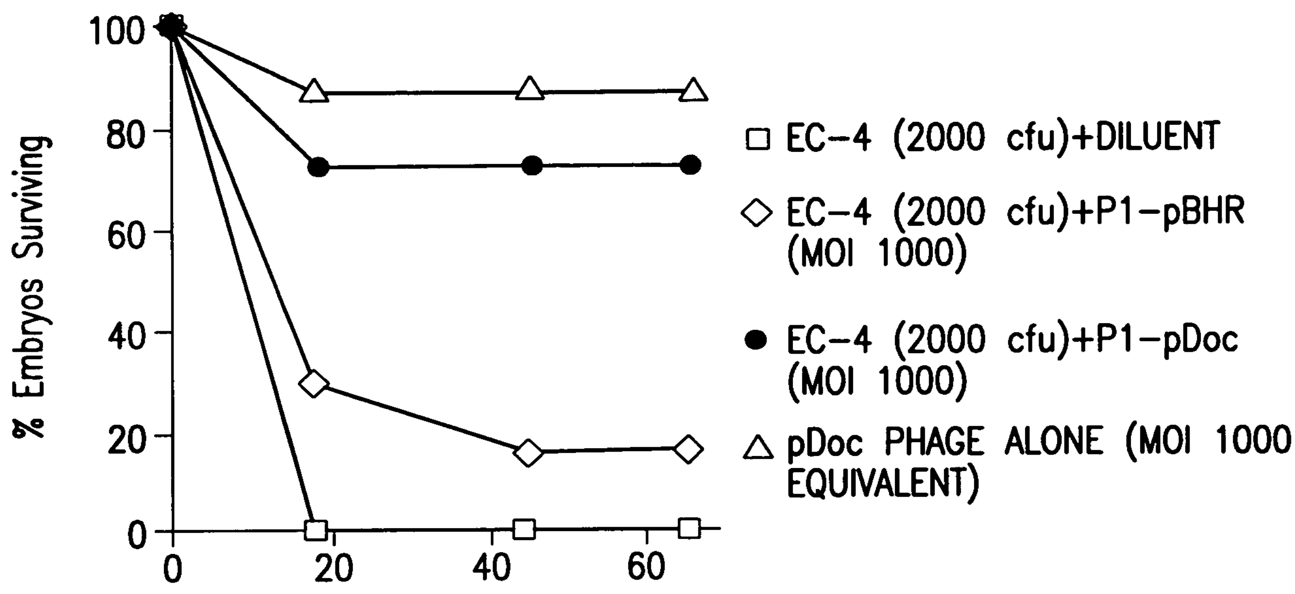

100
80
60
40
20
0
% Embryos Surviving
0
20
40
60
EC-4 (2000 cfu)+DILUENT
EC-4 (2000 cfu)+P1-pBHR (MOI 1000)
EC-4 (2000 cfu)+P1-pDoc (MOI 1000)
pDoc PHAGE ALONE (MOI 1000 EQUIVALENT)

FIG.17

5'–CAGGCGACAGGTATAGTTTCTCTCCGATTTGTGCCTGTCGCCTGC

FIG.18

pCLIP TRIPLE RIBOZYME STRUCTURE
INTERNAL RIBOZYME INSERT

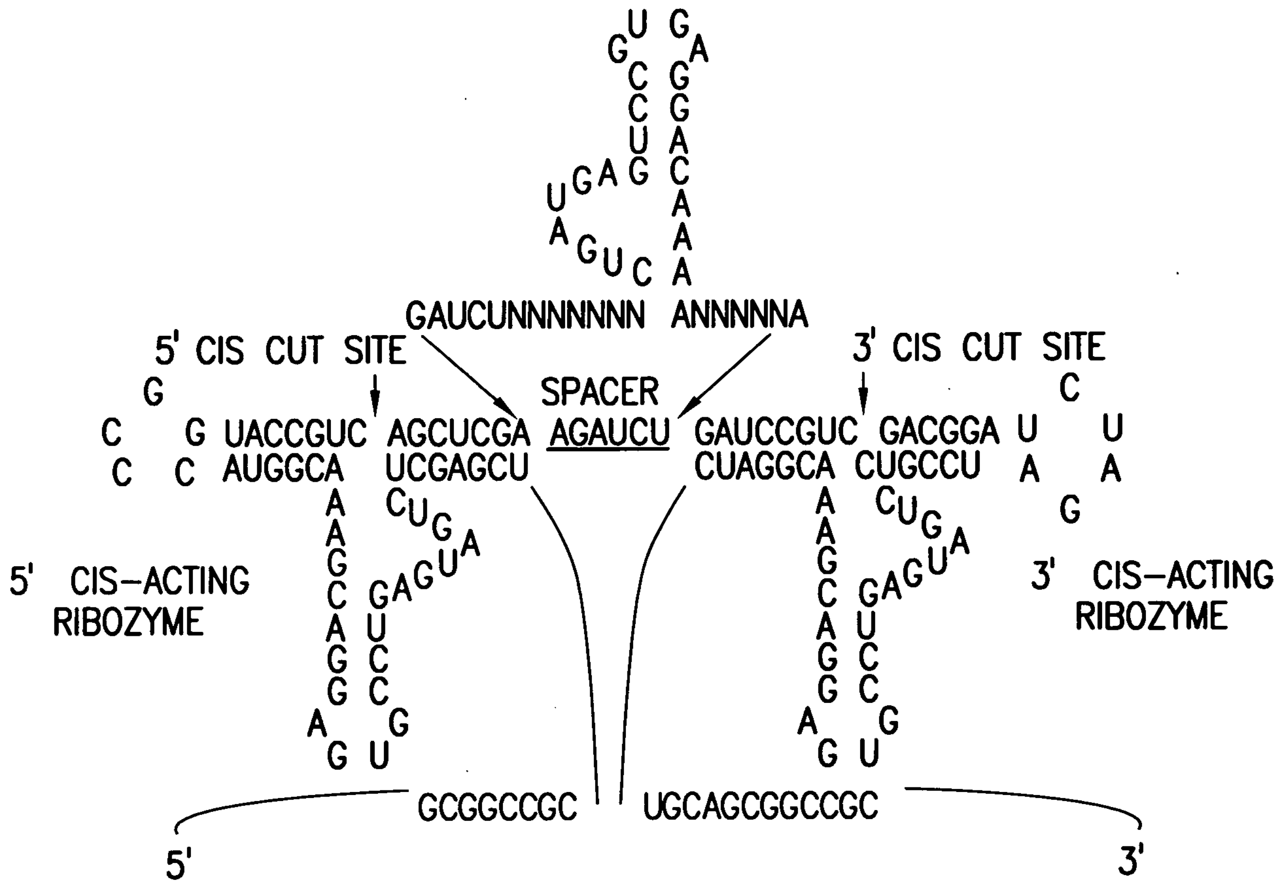


FIG.19

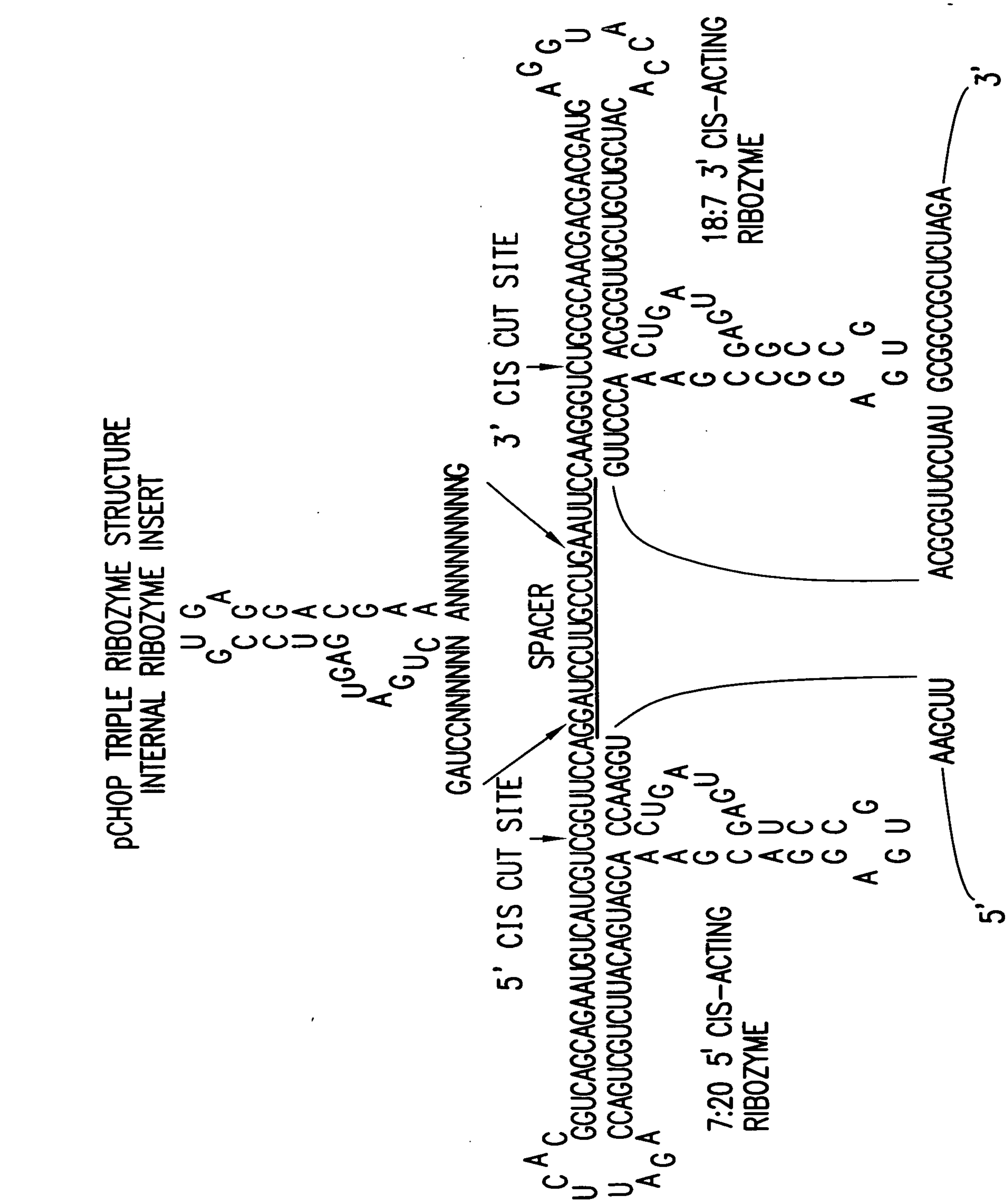

pCHOP TRIPLE RIBOZYME STRUCTURE
INTERNAL RIBOZYME INSERT
GAUCCNNNNNN ANNNNNNNNNG
5' CIS CUT SITE
SPACER
3' CIS CUT SITE
7:20 5' CIS-ACTING RIBOZYME
18:7 3' CIS-ACTING RIBOZYME
5'
3'

FIG.20

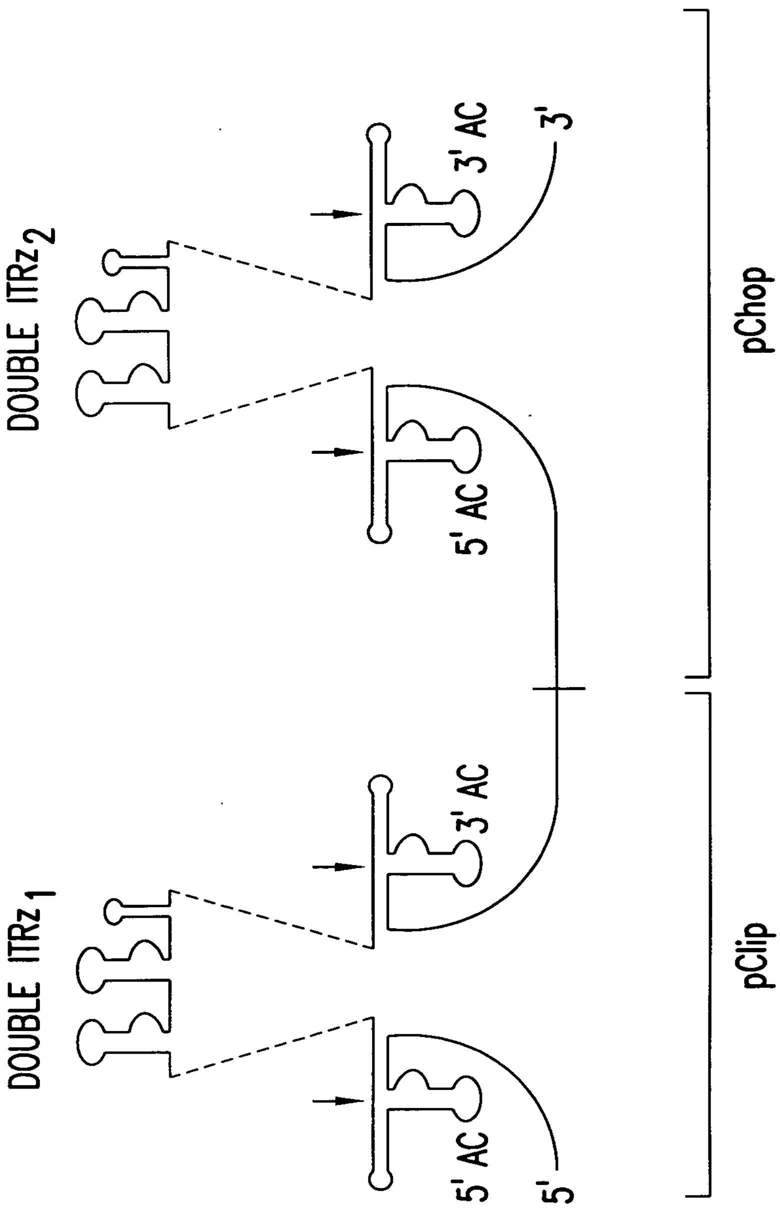


FIG.21

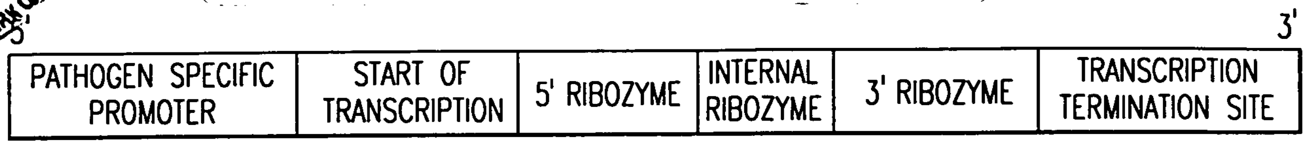


FIG.22A

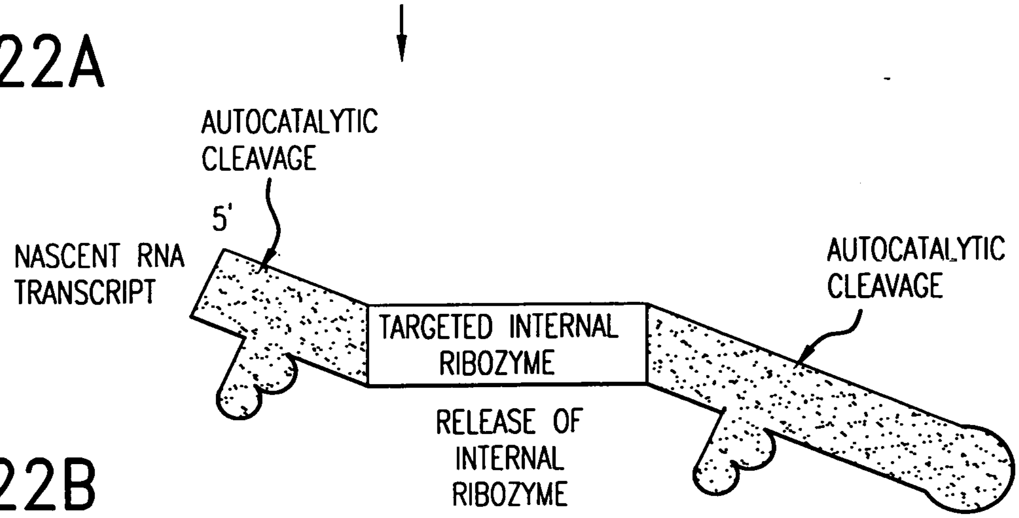


FIG.22B

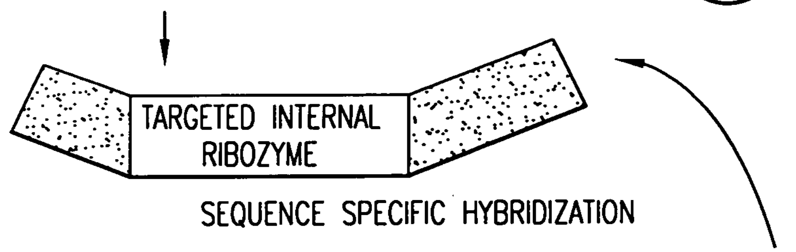


FIG.22C

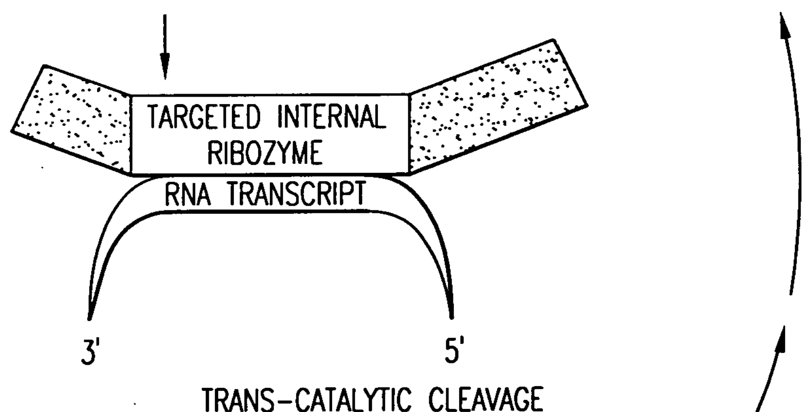


FIG.22D

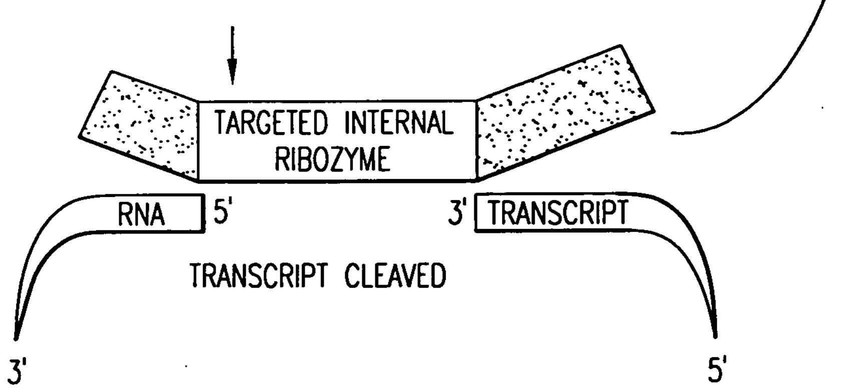


FIG.22E